Dermatology and Syphilology

THE Power for Good and Evil of Arsenic as a Remedy for Skin Diseases—The first knowledge of the specific pharmacodynamic effects of arsenic on the skin was gathered from observations on arsenic eaters, and from reports of various epidemics of arsenic poisoning.

Dermatologists learned long ago to restrict the use of arsenic to certain groups of chronic dematoses such as lichen planus, dermatitis herpetiformis, leucaemias. Its use in chronic eczemas is abandoned; in psoriasis it is used much less than before; and in acute dermatoses its use is considered definitely contraindicated.

The outstanding effect of arsenic on the skin is the exaggeration and stimulation of all nutritional and functional activities. Of these we are concerned here with the tendency of arsenic to stir up inflammatory dermatoses of eczematoid type.

The first notice of this type of arsenic reaction was served on the profession with the advent of the arsphenamine therapy in syphilis, particularly where used as a routine procedure in courses and series of a certain number of injections. Exfoliating arsenical dermatitis with exceedingly grave reactions and a number of fatalities were reported. Fortunately, however, in 1920 the important discovery made by Ravaut of France, and introduced in this country by McBride and Dennie, that sodium thiosulphate is a chemical antidote of arsenic has decreased but by no means removed exfoliating dermatitis from the dreaded and fatal episodes in the lives of syphilitics.

The statement will bear repetition that many of these consequences can be prevented if the physician will look for and detect the first prodromal and warning signs of the arsenical intolerance and the impending danger. These signs, as so ably portrayed by John Stokes, are: (1) small punctate subcuticular flush about the trunk, neck and flexures on the day following the injection; (2) patches of dermatitis at the flexures, upon the shins, or the face. These may be present for some days or even a week before the explosion; (3) severe itching of the skin on the day following the injection; (4) scarlatinoform or morbilliform erythemas.

A new and further important observation has been made by Throne, Van Dyck and associates,[2] who have reported a series of eczema cases in which the history was suggestive of a possibility of arsenic absorption through food, environmental or occupational channels. They treated these patients with intravenous injections of sodium thiosulphate and were able not only to clear up the skin lesions, but also to demonstrate the elimination of arsenic in the urine. Further elaboration of this observation may prove valuable in many other cases of chronic eczema with seemingly obscure etiology; and it also adds another emphatic reminder of the potentially powerful irritating effects of arsenic on the skin.

MOSES SCHOLTZ.

1. J. Stokes: Modern Clinical Syphilology, 1926.
2. Throne, Van Dyck, etc.: New York State Journal of Medicine, October 15, 1926.

Endocrinology

IODIN Therapy in Neurocirculatory Asthenia—During the World War physicians of all participating nations were puzzled by a symptom complex which manifested itself in many thousands of soldiers. It received various appellations: "irritable heart," "effort syndrome," "neurocirculatory asthenia," "autonomic imbalance," and "sympathicotonia." Many of the symptoms mimicked the clinical picture of Graves' disease in mild form, namely, palpitation, tachycardia, tremor, sweating, nervousness, excitability and irritability, insomnia, and lack of energy. Loss of weight was exceptional, although the majority of such individuals were apt to be undernourished rather than obese. Goiter was sometimes noted, but whether it was coincidental or related to the syndrome remained uncertain; at any rate the goiter was not of the hyperplastic variety (highly vascular with thrill and bruit characteristic of Graves' disease). Exophthalmus and the so-called thyroid eye signs were usually absent and, if present, were rarely pronounced. The basal metabolic rate was almost always normal. Occasionally a slight elevation was recorded (15 to 25 per cent plus). Repetition of the test usually disclosed a normal rate.

This syndrome is frequently encountered in civil life, especially in girls and young women and sometimes in men. Many of these patients have been regarded as victims of mild Graves' disease; some of them, therefore, have received inhibitory roentgen therapy to the thyroid gland; others have been subjected to partial thyroidectomy. Such treatment almost uniformly has failed to relieve the symptoms. The hypothesis of an hyperthyroidism as the fundamental cause seemed to be erroneous.

It was equally unsatisfactory, and futile, to dismiss these patients with a diagnosis of neurasthenia. Digitalis had but little influence on the tachycardia or subjective symptoms. Sedatives, such as bromides, were rarely effective and at best provided only temporary relief. Relatively slight emotional strain rather than physical effort evoked or exaggerated the syndrome, and yet psychotherapy, or "skillful neglect," proved less satisfactory than might have been anticipated. Rest cures, change of climate, ocean voyages, and all the gamut of medical artistry accomplished but little for this group of patients.

Critical opinion had about dismissed the idea of thyroid accountability when Kessel and Hyman, about two years ago, advanced the thesis that autonomic imbalance and Graves' disease were practically identical except for the absence in the former, and the presence in the latter, of an increased basal metabolism. Indeed they conceived of autonomic imbalance as a preliminary stage of Graves' disease and claimed that they had actually witnessed this transformation.

In the past few weeks the question has been reopened by an interesting contribution from Strouse and Binswanger[1] of Chicago. In a preliminary report of fifty cases, thirty-two of which had been "carried through long enough to permit of analytic study"; they announce that iodin medication produced remarkable and prompt relief of the symp-

1. Jour. Amer. Med. Assoc., 1927, 88, 161-164.

toms. They believe, therefore, that this syndrome is associated with iodin deficiency. Moreover, the iodin treatment did not affect the metabolic rate. They are inclined to the idea that effort-syndrome (neurocirculatory asthenia, etc.) is due to some temporary derangement of thyroid function, and the writer agrees with them that a normal metabolic rate does not exclude thyroid disturbance.

The precise rôle of iodin therapy even in the well-recognized forms of thyroid disease is by no means settled. Its usefulness in the prophylaxis of endemic goiter has been abundantly confirmed. It is often effective in causing simple adolescent goiter to disappear. Its revival in recent years in the treatment of Graves' disease has been most interesting. There can be no doubt that in exophthalmic goiter iodin therapy causes a prompt and precipitate drop in the basal metabolic rate with striking improvement in many symptoms, and that its preoperative use in this disease helps to avoid postoperative thyroid crises and consequently reduces the surgical mortality. Its indefinite use in Graves' disease over a long period of time is not so beneficial and indeed may at times be harmful. Its administration in adenomatous goiter is supposed to be contraindicated though some dispute this. And now it is recommended for the symptoms of autonomic imbalance.

One must admit that this iodin beneficence in such diverse though related states, remains perplexing. But whatever the ultimate explanation may be, it will be a boon to a multitude of people if further experience with iodin corroborates the report of Strouse and Binswanger and relieves the symptoms of neurocirculatory asthenia.

H. Lisser.

Do All Forms of Tetany Depend on a Parathyroid-Calcium Disturbance?—The intimate association of laboratory investigation with clinical application is perfectly illustrated in the treatment of tetania parathyreopriva and conditions which simulate it closely.

Many theories of the pathogenesis of tetany have been promulgated. These vary from the assumption that a simple toxemia is the responsible agent, to elaborate explanations based on complex changes in the chemistry of the blood. McCallum stated several years ago that there may be several types of tetany differing widely in their etiology and in the mechanism of their production, although the final changes in the blood which bring about the actual symptoms may be the same.

The isolation by Collips, early in 1925, of a parathyroid hormone, which definitely influences calcium metabolism as evidenced by its effect on the blood serum calcium, has given renewed impetus to the metabolic study of the various inorganic constituents of the body. In most, but by no means all of the various types of tetany there is a reduction in the calcium content of the blood serum, and inasmuch as a paucity of calcium produces an hyperexcitability of the nerve cells, considerable interest has been manifested by various investigators in the metabolism of calcium.

Scott and Usher [1] have recently reported the results of their studies on the etiology and hematology of twenty-one cases of infantile tetany. One of the important results of this observation indicates that disordered calcium metabolism is not always indicated by changes in the calcium content of the blood serum and that there may be a defective utilization of calcium by the body even when the amount of that element in the food or blood is normal. They cited two cases in which infantile tetany occurred despite a normal blood serum calcium. On the other hand, if the fact that a reduction in the calcium ion concentration of the neuron results in an hyperexcitability, it must be assumed that in certain instances at least an actual diminution of calcium ion does not occur despite a marked lowering of that element in the blood serum, for the writer has seen at least one case in which the blood serum calcium was reduced to the extremely low figure of 5.5 mg. per 100 cc. (a case of severe alkalosis) without the usual manifestations of tetany being apparent.

Obviously then there must be some factor other than the actual lowering of the calcium content of the blood serum which produces the profound hyperexcitability of the entire nervous system associated with the clinical syndrome of tetany. Wells has stated that the calcium salts are held partly in solution, partly in protein suspension, and partly in the form of calcium ion protein compounds. It is probable then that even though the blood serum calcium content is normal, as in gastric tetany and in the tetany resulting from hyperpnea, the calcium is not available for use by the body. In other words, the determination of the ionized calcium rather than the total calcium is a procedure which must be investigated thoroughly before it is possible to properly evaluate the various theories of the pathogenesis of tetany.

The writer ventures to predict that eventually it will be determined that the hormone as isolated by Collip affects the calcium content of the serum only secondarily, the primary effect being in some way associated with the ionization of calcium. Such a condition would simplify the explanation of tetany and give very strong support to the unitary pathogenesis of all forms of tetany, the underlying factor being a metabolic disturbance which produces a reduction of *calcium ions* from the neurons, no matter by what means.

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1. Journ. A. M. A., 87-1904, 1926.

Gastrointestinal Disorders

Jaundice—Jaundice results from staining of the tissues with bile pigment. Bile pigment, or bilirubin, is a product of hemoglobin catabolism. Although there have been supporters of the extrahepatic as well as the hepatic formation of bile pigment, it was pretty generally accepted until recently that the liver was essential for bile pigment production. However, with improved methods as applied by Whipple, Rich, Mann and others, it is now definitely established that under normal conditions bilirubin is formed in the liver, spleen and bone marrow, and apparently in no other organs or tissues. With bilirubin produced in the bone marrow, spleen